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Claims

1. A single-chain multi-functional polypeptide comprising
   (a) a first domain comprising a binding-site of an immunoglobulin chain or an antibody specifically recognizing the CD19 antigen; and
   (b) a second domain comprising a binding site of an immunoglobulin chain or an antibody specifically recognizing the human CD3 antigen.

2. The polypeptide of claim 1, wherein said two domains are connected by a polypeptide linker.

3. The polypeptide of claim 1 ~~or 2,~~ wherein said first and/or second domain mimic or correspond to a V_H and V_L region from a natural antibody.

4. The polypeptide of ~~any one of claims 1 to 3~~ claim 3, wherein said antibody is monoclonal antibody, synthetic antibody, or humanized antibody.

5. The polypeptide of ~~any one of claims 1 to 4~~ claim 4, wherein at least one of said domains is a single-chain fragment of the variable region of the antibody.

6. The polypeptide of ~~any one of claims 1 to 5~~ claim 1, wherein said domains are arranged in the order V_LCD19-V_HCD19-V_HCD3-V_LCD3.

7. The polypeptide of ~~any one of claims 2 to 6~~ claim 2, wherein said polypeptide linker comprises a plurality of glycine, alanine ~~and/or~~ serine residues or combinations thereof.

8. The polypeptide of ~~any one of claims 2 to 7~~ claim 2, wherein said polypeptide linker comprises a plurality of consecutive copies of an amino acid sequence.

claim 7

9. The polypeptide of ~~any one of claims 2 to 8~~, wherein said polypeptide linker comprises 1 to 5 amino acid residues.

claim 9

10. The polypeptide of ~~any one of claims 2 to 9~~, wherein said polypeptide linker comprises the amino acid sequence Gly Gly Gly Gly Ser.

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11. The polypeptide of any one of claims 1 to 10, wherein said first domain comprises at least one CDR of the V_H and V_L region comprising the amino acid sequence encoded by the DNA sequence depicted in Figure 8 from nucleotides 82 to 414 (V_L) and nucleotides 460 to 831 (V_H) and/or wherein said second domain comprises at least one CDR of the V_H and V_L region comprising the amino acid sequence encoded by the DNA sequence depicted in Figure 8 from nucleotides 847 to 1203 (V_H) and nucleotides 1258 to 1575 (V_L).

claim 1

12. The polypeptide of ~~any one of claims 1 to 11~~, wherein

(a) said binding site of the first domain has an affinity of at least about 10^{-7} M; and/or

(b) said binding site of the second domain has an affinity of less than about 10^{-7} M.

claim 1

13. The polypeptide of ~~any one of claims 1 to 12~~ that is a bispecific single-chain antibody.

claim 1

14. The polypeptide of ~~any one of claims 1 to 13~~, comprising at least one further domain.

15. The polypeptide of claim 14, wherein said further domain is linked by covalent or non-covalent bonds.

16. The polypeptide of claim 14 ~~or 15~~, wherein said at least one further domain comprises an effector molecule having a conformation suitable for biological

activity, capable of sequestering an ion or selective binding to a solid support or to a preselected determinant.

17. A polynucleotide which upon expression encodes a polypeptide of any one of claims 1 to 16.

18. A vector comprising the polynucleotide of claim 17.

19. A cell transfected with the polynucleotide of claim 17 or the vector of claim 18.

20. A method for the preparation of the polypeptide of any one of claims 1 to 16 which process comprises cultivating a cell of claim 19 and isolating said polypeptide from the culture.

21. A composition comprising the polypeptide of any one of claims 1 to 16, the polynucleotide of claim 17 or the vector of claim 18.

22. The composition of claim 21 which is a pharmaceutical composition optionally further comprising a pharmaceutically acceptable carrier.

23. The composition of claim 21, which is a diagnostic composition optionally further comprising suitable means for detections.

24. Use of the polypeptide of any one of claims 1 to 16, the polynucleotide of claim 17 or the vector of claim 18 for the preparation of a pharmaceutical composition for the treatment of B-cell malignancies, B-cell mediated autoimmune diseases or the depletion of B-cells.

25. The use of claim 24, wherein said B-cell malignancy is non-Hodgkin lymphoma.

~~26. Use of the polynucleotide of claim 17 or the vector of claim 18 for the preparation of compositions for gene therapy.~~

27. A method for identifying activators or inhibitors of T-cell activation or stimulation comprising
   (a) culturing T-cells and CD19 positive cells, ~~preferably B-cells,~~ in the presence of a polypeptide of ~~any one of claims 1 to 16~~ claim 1 and optionally in the presence of a component capable of providing a detectable signal in response to T-cell activation with a compound to be screened under conditions to permit activation of the T-cell, and
   (b) detecting the presence or absence of the signal generated from the interaction of the compound with the cells.

28. A method for the production of a pharmaceutical composition comprising the steps of the method of claim 27 and formulating the compound identified in step (b) in a pharmaceutically acceptable form.

29. The method according to claim 28 ~~or 29~~, wherein the compound identified in step (b) is modified by peptidomimetics.

~~30. A method for the treatment of B-cell malignancies, B-cell mediated autoimmune diseases or the depletion of B-cells comprising introducing the polypeptide of any one of claims 1 to 16, the polynucleotide of claim 17 or the vector of claim 18 into a human affected by said malignancies or disease.~~

~~31. A method for delaying a pathological condition which is caused by B-cell disorders, comprising introducing the polypeptide of any one of claims 1 to 16, the polynucleotide of claim 17 or the vector of claim 18 into a human affected by said pathological condition.~~